1.3.2 PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

IMMAVOR 200 mg (powder for solution for injection)

Voriconazole

Sugar free

Read all of this leaflet carefully before you are given IMMAVOR

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.

What is in this leaflet:

1. What IMMAVOR is and what it is used for

IMMAVOR contains the active substance voriconazole. IMMAVOR is an antifungal medicine. It works by killing or stopping the growth of the fungi that cause infections.

It is used for the treatment of patients (adults and children over the age of 2) with:

- invasive aspergillosis (a type of fungal infection due to *Aspergillus sp*),
- candidaemia (another type of fungal infection due to *Candida sp*) in non-neutropenic patients (patients without abnormally low white blood cells count),
- serious invasive *Candida sp.* infections when the fungus is resistant to fluconazole (another antifungal medicine),
- serious fungal infections caused by *Scedosporium sp.* or *Fusarium sp*. (two different species of fungi).

IMMAVOR is intended for patients with worsening, possibly life-threatening, fungal infections.

Prevention of fungal infections in high-risk bone marrow transplant recipients.

This product should only be used under the supervision of a doctor.

2. What you need to know before you receive IMMAVOR

IMMAVOR should not be administered to you:

- If you are allergic to the active ingredient voriconazole, or to or any of the other ingredients of IMMAVOR (listed in section 6).
- If you are pregnant or breastfeeding
- If you have severe liver disease (severe impairment of hepatic function)

It is very important that you inform your doctor or pharmacist if you are taking or have taken any other medicines, even those that are obtained without a prescription, or herbal medicines.

The medicines in the following list must not be taken during your IMMAVOR treatment:

- Terfenadine (used for allergy)
- Astemizole (used for allergy)
- Cisapride (used for stomach problems)
- Pimozide (used for treating mental illness)
- Quinidine (used for irregular heart beat)
- Ivabradine (used for chronic heart failure)
- Rifampicin (used for treating tuberculosis)
- Efavirenz (used for treating HIV) in doses of 400 mg and above once daily
- Carbamazepine (used to treat seizures)
- Phenobarbital (used for severe insomnia and seizures)

- Ergot alkaloids (e.g., ergotamine, dihydroergotamine; used for migraine)
- Sirolimus (used in transplant patients)
- Ritonavir (used for treating HIV) in doses of 400mg and more twice daily
- Rifabutin (used to treat tuberculosis)
- St. John's Wort (herbal supplement)
- Venetoclax (used to treat a certain type of cancer)

Warnings and precautions

Tell your doctor or health care provider before being given the injection:

- If you have had an allergic reaction to other azoles.
- If you plan to be pregnant
- you are suffering from or have ever suffered from liver disease. If you have liver disease, your doctor may prescribe a lower dose of IMMAVOR. Your doctor should also monitor your liver function while you are being treated with IMMAVOR by doing blood tests.
- you are known to have cardiomyopathy, irregular heart beat, slow heart rate or an abnormality of electrocardiogram (ECG) called 'long QTc syndrome'.

You should avoid any sunlight and sun exposure while being treated. It is important to cover sun exposed areas of skin and use sunscreen with high sun protection factor (SPF), as an increased sensitivity of skin to the sun's UV rays can occur. These precautions are also applicable to children.

While being treated with IMMAVOR:

tell your doctor immediately if you develop

- o sunburn
- o severe skin rash or blisters
- o bone pain

If you develop skin disorders as described above, your doctor may refer you to a dermatologist, who after consultation may decide that it is important for you to be seen on a regular basis. There is a small chance that skin cancer could develop with long-term use of IMMAVOR.

Your doctor should monitor the function of your liver and kidney by doing blood tests.

Children and adolescents

IMMAVOR should not be given to children younger than 2 years of age.

Other medicines and IMMAVOR

Tell your doctor, pharmacist, or nurse if you are taking, have recently taken or might take any other medicines, including those that are obtained without a prescription

Some medicines, when taken at the same time as IMMAVOR, may affect the way IMMAVOR works or IMMAVOR may affect the way they work.

Tell your doctor if you are taking the following medicine, as treatment with IMMAVOR at the same time should be avoided if possible:

- Ritonavir (used for treating HIV) in doses of 100 mg twice daily

Tell your doctor if you are taking either of the following medicines, as treatment with IMMAVOR at the same time should be avoided if possible, and a dose adjustment of IMMAVOR may be required:

- Rifabutin (used for treating tuberculosis). If you are already being treated with rifabutin your blood counts and side effects to rifabutin will need to be monitored.
- Phenytoin (used to treat epilepsy). If you are already being treated with phenytoin your blood concentration of phenytoin will need to be monitored during your treatment with IMMAVOR and your dose may be adjusted.

Tell your doctor if you are taking any of the following medicines, as a dose adjustment or monitoring may be required to check that the medicines and/ or IMMAVOR are still having the desired effect:

- Warfarin and other anticoagulants (e.g., phenprocoumon, acenocoumarol; used to slow down clotting of the blood)
- Ciclosporin (used in transplant patients)
- Tacrolimus (used in transplant patients)
- Sulfonylureas (e.g., tolbutamide, glipizide, and glyburide) (used for diabetes)
- Statins (e.g., atorvastatin, simvastatin) (used for lowering cholesterol)
- Benzodiazepines (e.g., midazolam, triazolam) (used for severe insomnia and stress)
- Omeprazole (used for treating ulcers)
- Oral contraceptives (if you take IMMAVOR whilst using oral contraceptives, you may get side effects such as nausea and menstrual disorders)
- Vinca alkaloids (e.g., vincristine and vinblastine) (used in treating cancer)
- Indinavir and other HIV protease inhibitors (used for treating HIV)
- Non-nucleoside reverse transcriptase inhibitors (e.g., efavirenz, delavirdine, nevirapine) (used for treating HIV) (some doses of efavirenz can NOT be taken at the same time as IMMAVOR)
- Methadone (used to treat heroin addiction)
- Alfentanil and fentanyl and other short-acting opiates such as sufentanil (painkillers used for surgical procedures)
- Oxycodone and other long-acting opiates such as hydrocodone (used for moderate to severe pain)
- Non-steroidal anti-inflammatory drugs (e.g., ibuprofen, diclofenac) (used for treating pain and inflammation)
- Fluconazole (used for fungal infections)
- Everolimus (used for treating advanced kidney cancer and in transplant patients)

Pregnancy, breast-feeding and fertility

IMMAVOR must not be used during pregnancy. Effective contraception must be used in women of childbearing potential. Contact your doctor immediately if you become pregnant while being treated with IMMAVOR.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

Driving and using machines

IMMAVOR may cause blurring of vision or uncomfortable sensitivity to light. While affected, do not drive or operate any tools or machines. Tell your doctor if you experience this.

It is not always possible to predict to what extent IMMAVOR may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which IMMAVOR affects them.

3. **How** IMMAVOR **is given**

Your doctor will determine your dose depending on your weight and the type of infection you have.

You will be given IMMAVOR by intravenous infusion (into a vein).

Your doctor will determine the dose and duration of your treatment with IMMAVOR.

You may be switched from the intravenous infusion to tablets once your condition improves.

If you think that the effect of IMMAVOR is too strong, or that it does not seem to be working, tell your doctor or pharmacist.

If you are given more IMMAVOR **than you should:**

Since IMMAVOR Infusion is given by a doctor or nurse, it is very unlikely that you will be given too much of the medicine. If you think that you have been given too much IMMAVOR, tell a doctor or nurse at once.

Since a health care provider will administer IMMAVOR, he / she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you missed a dose of IMMAVOR**:**

As you will be given this medicine under close medical supervision, it is unlikely that a dose would be missed. However, tell your doctor of pharmacist if you think that a dose has been forgotten.

4. Possible side effects

Not all side effects reported for IMMAVOR are included in this leaflet. Should your general health worsen while taking IMMAVOR, please consult your doctor, pharmacist or other healthcare professional for advice.

IMMAVOR can have side effects. If any side effects occur, most are likely to be minor and temporary. However, some may be serious and need medical attention.

Frequent side effects are:

- Visual disturbances (change in vision)
- Fever
- Rash
- Nausea, vomiting, diarrhoea
- Headache
- Swelling of the extremities
- Stomach pains
- Flu-like symptoms, sinusitis, chills, weakness
- Anaemia, low numbers of cells called platelets that help the blood to clot, low numbers of some types of white blood cells or of all types of blood cells, red or

purple discoloration of the skin which may be caused by low platelet count, other blood cell changes

- Low blood sugar, low blood potassium
- Anxiety, depression, tingling, confusion, dizziness, agitation, trembling, hallucinations and other nervous symptoms.
- Low blood pressure, inflammation of a vein (which may be associated with the formation of a blood clot)
- Breathing difficulty, chest pain, fluid accumulation in the lungs
- Jaundice, redness of the skin
- Swelling of the lips or face
- Dyspepsia (heartburn/indigestion)
- Constipation
- Gingivitis (inflammation of the gums)
- Gastroenteritis (inflammation of gastrointestinal tract)
- Allergic reactions (sometimes severe), including widespread blistering rash and skin peeling, severe skin reaction following exposure to light or sun
- Itchiness
- Hair loss
- Back pain
- Kidney failure, blood in the urine, changes in blood tests of kidney function
- Inflammation at injection sites
- Hepatitis (inflammation of the liver)
- Changes in blood tests of liver function

Less frequent side effects are:

- Enlarged lymph glands (sometimes painful)

- Increase in a type of white blood cell which may be associated with allergic reaction, disorder of blood clotting system
- Heart rhythm problems including very fast heartbeat, very slow heartbeat, fainting
- Depressed function of the adrenal gland
- Problem with coordination
- Manifestation (signs) of swelling of the brain
- Double vision pain and inflammation of the eyes and eyelids, involuntary movement of the eye
- Underactive thyroid gland
- Decreased sensitivity to touch
- Pancreatitis (inflammation of the pancreas), peritonitis (inflammation of the lining of the abdominal cavity)
- Swelling and inflammation of the tongue
- Enlarged liver, liver failure, gallbladder disease, gallstones
- Joint pain
- Inflammation of the kidney, proteins in the urine
- Abnormal electrocardiogram (ECG)
- Blood chemistry changes
- Inability to sleep
- Hearing difficulties, ringing in the ears
- Abnormal sense of taste
- Increase in muscle tone, muscle weakness caused by an abnormal immune system response
- Abnormal brain function, Parkinson-like symptoms, convulsion
- Sleepiness during infusion
- Allergic skin reactions (sometimes severe)

- Eczema (red, itchy skin)
- Psoriasis (scaly, itchy, dry patches of skin)
- Increased blood urea
- Increased blood cholesterol

Other side effects

• Low sodium in the blood

• Skin cancer

• Red, scaly patches or ring-shaped skin lesions that may be a symptom of an autoimmune disease called cutaneous lupus erythematosus

Reactions during the infusion have occurred uncommonly with IMMAVOR (including flushing, fever, sweating, increased heart rate and shortness of breath). Your doctor may stop the infusion if this occurs.

As IMMAVOR has been known to affect the liver and the kidney, your doctor should monitor the function of your liver and kidney by doing blood tests. Please advise your doctor if you have any stomach pains or if your stools have a different consistency.

If any of these side effects persist or are troublesome, please tell your doctor.

If you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of IMMAVOR

5. How to store IMMAVOR

Store all medicines out of reach of children.

Store at or below 25 °C

Store in the original package to protect from light.

Contents of the pack and other information

What IMMAVOR contains

- The active substance is voriconazole
- The other ingredient is Betadex Sulfobutyl Ether Sodium

What IMMAVOR looks like and contents of the pack

IMMAVOR is a white, lyophilised powder in 25 ml clear Type I glass vial with 20 mm grey bromobutyl slotted rubber stopper and sealed with 20 mm red colour grain finish aluminium flip-off seal in unit carton. Packs of 1, 5 or 10

Not all pack sizes may be marketed

Holder of Certificate of Registration

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